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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/849,518	05/20/2004	Gregory D. Plowman	034536-1595	7215

22428 7590 06/06/2005

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
YAO, LEI	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/849,518	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/20/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-12 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/16/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *exhibit A and B*.

DETAILED ACTION

This office action is written in response to the document received 5/20/2004.

Claims 1-9 and 13-22 have been cancelled. Claims 10-12 and 23-27 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Drawn to written Description

Claims 10-12 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 10-12 and 23-27 are inclusive of genus of "ALK-7 polypeptides", polypeptide containing fragments, the domains, region, of SEQ ID NO: 2 ", and "the amino acid sequence that is at least 95% identical to the sequence of SEQ ID NO: 2". The claims encompass significant structural dissimilarity and diversity as compared to the ALK-7 protein (SEQ ID NO: 2).

The specification teaches that an ALK-7 polypeptide can be encoded by a full-length nucleic acid sequence or any protein of the full-length nucleic acid sequence (page 9). The specification also teaches that polypeptide of the invention comprises an amino acid sequence containing fragments, portion, domain (page 22). However, the written description (specification, pages 98-100) only reasonably conveys KA-tagged ALK-7, the ALK-7DN, and ALK-7TD proteins in associated with the activity in growth and/or survival of neurons and neurodegenerative disease. A description of a genus may be achieved by

means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus. Although drawn to DNA arts, the finding in University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) is relevant to the instant claims. The Federal Circuit addressed "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification does not provide an enough representative number of polypeptides that encompass the genus of ALK-7 polypeptides characterized to have neuron growth and survival activity. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of KA-tagged ALK-7, the ALK-7DN, and ALK-7TD proteins is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polypeptides of ALK-7, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a

potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only the complete ALK protein, KA-tagged ALK-7, the ALK-7DN, and ALK-7TD proteins, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Drawn to Enablement

Claims 10-12 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the complete ALK-7 protein, KA-tagged ALK-7, the ALK-7DN, and ALK-7TD proteins, in the growth and/or survival of neurons, does not reasonably provide enablement for any other variants, fragments, domains of ALK-7 protein or polypeptides of SEQ ID NO: 2 in the growth and/or survival of neurons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are broadly drawn to an isolated ALK-7 polypeptide set forth in SEQ ID NO: 2, portions, fragments and variants of in SEQ ID NO: 2. The specification teaches that ALK-7 polypeptide can be encoded by a full-length nucleic acid sequence or any portion of the full-length nucleic acid

sequence Page 9, line 20-23). The specification teaches that KA-tagged ALK-7, the ALK-7DN, and ALK-7TD proteins have activity in growth and/or survival of neurons (pages 98-100). However, the specification does not teach that any other fragment, portion, or variant of ALK-7 lacking or containing one of the domains above has neuron growth or survival activity. The specification does not teach any other variant, which is at least 95% identical to the SEQ ID NO: 2, has neuron growth or survival activity. The specification does not teach that any other fragment or variant of ALK-7 protein lacking or containing one of the domains above having any biological function as ALK-7 protein. The specification provides no working examples, which enable the any other fragment or variant of ALK-7 protein in the claims to perform a function for neuron growth or survival. Since the specification does not provide enough teaching on all claimed polypeptides having biological activity including neuron growth or survival. Since the specification does not provide any guidance for using polypeptides other than SEQ ID NO: 2, KA-tagged ALK-7, the ALK-7DN, and ALK-7TD, one skilled in the art would not know how to use the claimed polynucleotides on the basis of teachings in the prior art or instant specification.

It is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). The specific conformation of a protein results from non-covalent interactions between amino acids, beyond what is dictated by the primary amino acid sequence. It is known in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by aglutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990. Due to these reasons, one of skill in the art would be forced into undue experimentation in order to practice the invention as claimed.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to the activity of claimed fragment, domain, or variant of ALK-7 protein, one skilled in the art would be forced into under experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10, 11, 12 (b-d), 24, and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Ibanez et al., (US Patent NO: 5614609).

As written description in specification on page 9, line 20-23 "an ALK-7 polypeptide can be encoded by a full-length nucleic acid sequence or any portion of the full-length nucleic acid sequence", Claim 10-11 are interpreted as being drawn to an isolated ALK-7 polypeptide and fragment of the polypeptide, ALK-7, which has the amino acid sequence set forth in SEQ ID NO: 2. Claims 12 (b, c, d), 24 and 25 embody the claim 10, wherein the polypeptide comprising one or more of the domains of SEQ ID NO: 2 or except that it lacks of the domains of SEQ ID NO: 2.

Ibanez et al., disclose ALK-7 protein consisting of an amino acid sequence, which is 94.2% identical to the SEQ ID NO: 2, as evidenced by sequence search result (Exhibit A). Ibanez et al., disclose that Alk-7 can be used as protein marker for diagnosis for neurodegenerative disease (column 2, line 25-28).

Ibanez et al., (WO 9612805), also anticipated the claims evidenced by exhibit B.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Dowining for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

KAREN A. CANELLA PH.D
PRIMARY EXAMINER

```
  Matches  493;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60

Qy         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120

Qy        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180

Qy        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240

Qy        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300

Qy        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCETCAIADLGLAVKHDSILNTIDIPQN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420

Qy        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480

Qy        481 TISQLCVKEDCKA 493
              |||||||||||||
Db        481 TISQLCVKEDCKA 493


RESULT 2
US-08-341-916-2
; Sequence 2, Application US/08341916
; Patent No. 5614609
;  GENERAL INFORMATION:
;    APPLICANT:  Ib  ez, Carlos F.
;    APPLICANT:  Ryd n, Mikael
;    APPLICANT:  J rnvall, Henrik
;    TITLE OF INVENTION:  A No. 5614609el Serine Threonine Kinase Receptor
;    NUMBER OF SEQUENCES:  6
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Sterne, Kessler, Goldstein & Fox
;      STREET:  1100 New York Avenue, Suite 600
;      CITY:  Washington
;      STATE:  DC
;      COUNTRY:  USA
;      ZIP:  20005
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/341,916
;      FILING DATE:  Herewith
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Goldstein, Jorge A.
;      REGISTRATION NUMBER:  29,021
;      REFERENCE/DOCKET NUMBER:  1459.0230001
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (202)371-2600
;      TELEFAX:  (202)371-2540
;  INFORMATION FOR SEQ ID NO:  2:

;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  493 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-341-916-2

  Query Match          94.2%;  Score 2449;  DB 1;  Length 493;
  Best Local Similarity  93.1%;  Pred. No. 2.5e-240;
  Matches  459;  Conservative   19;  Mismatches   15;  Indels    0;  Gaps    0;

Qy          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60
              || |  ||| ||||:| |::|: ||||||||||||||||||||||||||||||||||||
Db          1 MTPASRSALSLALLLVALASDLAAGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60

Qy         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120
              ||||||||||||||||||||||||||||||||||||||||||:||:||| || ::|||
Db         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPDAPRLGPTELTVVITV 120

Qy        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180
              ||||||||||||:|||| |||:||| || ||||||:| :|||||||||||||| ||||||
Db        121 PVCLLSIAAMLTIWACQDRQCTYRKTKRHNVEEPLAEYSLVNAGKTLKDLIYDATASGSG 180

Qy        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240

Qy        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||:||||||||
Db        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMVKLALSIA 300

Qy        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCETCAIADLGLAVKHDSILNTIDIPQN 360
              ||||||||||||||||||||||||||||||||:||||||||||||||||:||||||||
Db        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCDTCAIADLGLAVKHDSIMNTIDIPQN 360

Qy        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||:|||||||||
Db        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGLVEEYQLPYYD 420

Qy        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480
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Db        421 MVPSDPSIEEMRKVVCDQKLRPNLPNQWQSCEALRVMGRIMRECWYANGAARLTALRVKK 480

Qy        481 TISQLCVKEDCKA 493
              |||||||||||||
Db        481 TISQLCVKEDCKA 493


RESULT 3
US-08-805-166-2
; Sequence 2, Application US/08805166
; Patent No. 5789565
;  GENERAL INFORMATION:
;    APPLICANT:  Ib  ez, Carlos F.
;    APPLICANT:  Ryd n, Mikael
;    APPLICANT:  J rnvall, Henrik
;    TITLE OF INVENTION:  A No. 5789565el Serine Threonine Kinase Receptor
;    NUMBER OF SEQUENCES:  6
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Sterne, Kessler, Goldstein & Fox
;      STREET:  1100 New York Avenue, Suite 600
;      CITY:  Washington
;      STATE:  DC
;      COUNTRY:  USA
;      ZIP:  20005
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/805,166
;      FILING DATE:  24-FEB-1997
```

Exhibit A

```
CC   substances that modulate their activity (i.e. agonists and antagonists,
CC   including NBP) in vivo or in vitro. These substances are used to treat or
CC   prevent diseases associated with abnormal signal transduction pathways
CC   that involve the proteins, particularly cancer (e.g. leukaemia and
CC   lymphoma), while modulators of ALK-7 (which is a type I receptor
CC   serine/threonine kinase) are used to promote neuronal survival,
CC   particularly for treating Alzheimer's, Parkinson's or Huntington's
CC   diseases. Nucleic acid fragments of the polynucleotides encoding the
CC   proteins can be used as probes to identify and clone related sequences;
CC   to detect protein-encoded RNA; to generate transgenic animals and in gene
CC   therapy (optionally after mutation). Ab are used to determine the
CC   proteins
XX
SQ   Sequence 493 AA;

  Query Match             100.0%;  Score 2601;  DB 2;  Length 493;
  Best Local Similarity   100.0%;  Pred. No. 7e-243;
  Matches  493;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60

Qy         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120

Qy        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180

Qy        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240

Qy        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300

Qy        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCETCAIADLGLAVKHDSILNTIDIPQN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCETCAIADLGLAVKHDSILNTIDIPQN 360

Qy        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420

Qy        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480

Qy        481 TISQLCVKEDCKA 493
              |||||||||||||
Db        481 TISQLCVKEDCKA 493


RESULT 2
AAR95562
ID   AAR95562 standard; protein; 493 AA.
XX
AC   AAR95562;
XX
DT   25-MAR-2003  (revised)
DT   27-AUG-1996  (first entry)
XX
DE   Serine threonine kinase receptor ALK-7.
XX
KW   Serine threonine kinase receptor; ALK-7; activin-like kinase-7;
KW   neurodegenerative disease; Alzheimer disease; stroke; cancer; infection;
KW   diagnosis; gene therapy; transgenic animal.
XX
OS   Rattus sp.

PN   WO9612805-A1.
XX
PD   02-MAY-1996.
XX
PF   20-OCT-1995;   95WO-IB000899.
XX
PR   20-OCT-1994;   94US-00325956.
PR   15-NOV-1994;   94US-00341916.
XX
PA   (IBAN/) IBANEZ C F.
XX
PI   Ibanez CF,  Ryden M,  Joernvall H;
XX
DR   WPI; 1996-230606/23.
DR   N-PSDB; AAT26994.
XX
PT   DNA encoding serine threonine kinase receptor, activin-like kinase-7 -
PT   useful to treat neurological disease, and to screen individuals at risk
PT   of disease associated with altered expression of ALK-7.
XX
PS   Claim 3; Page 56-57; 71pp; English.
XX
CC   A novel rat serine threonine kinase receptor, Alk-7 (activin-like kinase-
CC   7) (AAR95562), was identified as the product of a cDNA clone (AAT26994)
CC   isolated from a day 7 total rat brain library. It can be produced e.g. in
CC   transfected NIH3T3 cells carrying a vector incorporating an encoding
CC   sequence. Cells expressing the polypeptide are useful in bioassays to
CC   assess candidate drugs or ligands of the ALK-7 receptor. The polypeptide
CC   in a gene delivery system can be used to treat a neurological disease,
CC   partic. a neurodegenerative disease (e.g. Alzheimer disease), disorder or
CC   injury (e.g. stroke), neoplasia or infection. (Updated on 25-MAR-2003 to
CC   correct PI field.)
XX
SQ   Sequence 493 AA;

  Query Match             94.2%;  Score 2449;  DB 2;  Length 493;
  Best Local Similarity   93.1%;  Pred. No. 3.9e-228;
  Matches  459;  Conservative   19;  Mismatches   15;  Indels    0;  Gaps    0;

Qy          1 MTRALCSALRQALLLLAAAAELSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60
              || |  |||  ||||:| |::|: ||||||||||||||||||||||||||||||||||||
Db          1 MTPASRSALSLALLLVALASDLAAGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVI 60

Qy         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPNAPKLGPMELAIIITV 120
              ||||||||||||||||||||||||||||||||||||||||||:||:||| || ::|||
Db         61 KSCVSLPELNAQVFCHSSNNVTKTECCFTDFCNNITLHLPTASPDAPRLGPTELTVVITV 120

Qy        121 PVCLLSIAAMLTVWACQGRQCSYRKKKRPNVEEPLSECNLVNAGKTLKDLIYDVTASGSG 180
              |||||||||||||:|||| |||:||| || ||||||:| :|||||||||||||| ||||||
Db        121 PVCLLSIAAMLTIWACQDRQCTYRKTKRHNVEEPLAEYSLVNAGKTLKDLIYDATASGSG 180

Qy        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SGLPLLVQRTIARTIVLQEIVGKGRFGEVWHGRWCGEDVAVKIFSSRDERSWFREAEIYQ 240

Qy        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMIKLALSIA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||:|||||||
Db        241 TVMLRHENILGFIAADNKDNGTWTQLWLVSEYHEQGSLYDYLNRNIVTVAGMVKLALSIA 300

Qy        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCETCAIADLGLAVKHDSILNTIDIPQN 360
              |||||||||||||||||||||||||||||:|||||||||||||||||||:|||||||||||
Db        301 SGLAHLHMEIVGTQGKPAIAHRDIKSKNILVKKCDTCAIADLGLAVKHDSIMNTIDIPQN 360

Qy        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGIVEEYQLPYYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||:||||||||||
Db        361 PKVGTKRYMAPEMLDDTMNVNIFESFKRADIYSVGLVYWEIARRCSVGGLVEEYQLPYYD 420

Qy        421 MVPSDPSIEEMRKVVCDQKFRPSIPNQWQSCEALRVMGRIMRECWYANGAARLTALRIKK 480
              |||||||||||||||||| ||::|||||||||||||||||||||||||||||:||
Db        421 MVPSDPSIEEMRKVVCDQKLRPNLPNQWQSCEALRVMGRIMRECWYANGAARLTALRVKK 480

Qy        481 TISQLCVKEDCKA 493
              |||||||||||||
```

Exhibit B